AMENDMENTS TO THE SPECIFICATION

Please amend the paragraphs at page 9, line 25 through page 10, line 20, as follows.

1) HA salified with organic and/or inorganic bases;
2) ~~Hyaff~~ HYAFF®: esters of HA with alcohols of the aliphatic, araliphatic, cycloaliphatic, aromatic, cyclic and heterocyclic series, with a percentage of esterification that may vary according to the type and length of the alcohol used, preferably between 50 and 100%, while the remaining percentage of non-esterified HA may be salified with organic and/or inorganic bases (European patent No. 0216453 B1);
3) ~~Hyadd~~ HYADD™: amides of HA with amines of the aliphatic, araliphatic, cycloaliphatic, aromatic, cyclic and heterocyclic series, with a percentage of amidation of between 0.1 and 15%, while the remaining percentage of HA which has not undergone amidation may be salified with organic and/or inorganic bases (European patent application publication No. 1095064);
4) O-sulphated HA derivatives to the 4^{th} degree of sulphation (European patent No. 0702699 B1);
5) ACP®: inner esters of HA with a percentage of esterification lower than or equal to 20%, preferably between 0.05 and 5%, while the remaining percentage of non- esterified HA can be salified with organic and/or inorganic bases (European patent No. 0341745 B1);
6) Deacetylation products of HA: these derive from the deacetylation of the N-acetyl-glucosamine fraction with a percentage of deacetylation ranging preferably between 0.1 and 30%, while the carboxy groups of HA may be salified with organic and/or inorganic bases (international patent application PCT No. WO 02/18450);

7) ~~Hyoxx~~ HYOXX™: percarboxylated derivatives of HA obtained by the oxidation of the primary hydroxyl of the N-acetyl-glucosamine fraction with a degree of percarboxylation of between 0.1 and 100% and, preferably between 25 and 75%. All the carboxy groups of HA can be salified with organic and/or inorganic bases (international patent application PCT No. WO 02/18448).

The HA derivatives listed above that have proved to be particularly important in forming the new bone grafts are the esters of hyaluronic acid, preferably the benzyl ester (~~Hyaff~~ HYAFF®11), esterified to a percentage of between 50 and 100%, and preferably between 75 and 100%.

Please amend the paragraph at page 12, lines 8-21, as follows

The matrix inside the structure claimed by the present Applicant, may be constituted by 2 or more components and may therefore be in the form of a composite association of materials that are listed and described below:

- HA sodium salt, with a molecular weight of between 30 KD [[~~KDs~~]] and 1.5 X 10^3 KD [[~~KDs~~]], preferably from [[~~da~~]] 200 KD [[~~KDs a~~]] to 750 KD [[~~KDs~~]];
- HA derivatives such as esters (~~Hyaff~~ HYAFF®), inner esters (ACP®), percarboxylated derivatives (~~Hyoxx~~ HYOXX®), amides (~~Hyadd~~ HYADD™), sulphated and deacetylated HA derivatives. Said derivatives may be made into the form of fibres, powders, microspheres, sponges, pastes, gels and granules;
- bone matrix, totally or partially demineralised (DM);
- biodegradable, biocompatible and bioabsorbable materials such as hydroxyapatite, tribasic calcium phosphate and calcium sulphate;

- bone granules and/or powders of autologous, allogenic or animal origin, of various shapes and sizes.

Please amend the paragraph at page 13, lines 3-29, as follows.

3) sponges formed by the inner esters of HA (ACP®) containing between them bone granules and/or powders autologous and/or allogenic and/or of animal origin, or constituted by biodegradable ceramics or, lastly, sponges of ACP® containing DM.

4) granules, spheres, powders and/or two- and three-dimensional structures of various shapes and sizes constituted by biodegradable ceramics that are coated/incorporated in a layer of HA subsequently cross-linked to form its inner ester (ACP®) which thus covers all the ceramic structures described above.

5) pastes and/or gels constituted by HA derivatives enclosing bone powders and/or granules that are autologous and/or allogenic and/or of animal origin, or granules or other two- or three-dimensional structures constituted by biodegradable ceramics or, lastly, pastes and/or gels containing DM;

6) fibres constituted by the benzyl ester of HA (~~Hyaff~~ HYAFF® 11) (possibly also associated with other natural polymers and with the derivatives thereof such as collagen and cellulose, or synthetic polymers such as poly-lactic, polyglycolic and poly-caprolactone acid) with a percentage of esterficiation ranging between 50 and 100%, preferably 75% (~~Hyaff~~ HYAFF® 11p75), in association with DM and hyaluronic acid, preferably sodium salt, for the formation of a compact paste as a matrix to insert between two layers as described earlier. The matrix can be wetted with a solution of ~~Hyaff~~ HYAFF®, to render it more compact with the layers between which it is sandwiched. The percentage of said matric composed of fibres of ~~Hyaff~~ HYAFF® 11p75 may vary between 10 and 50%, but is preferably between 14 and 24%. The

percentage of DM in the composition of the matrix may vary between 50 and 90%, preferably between 60 and 80%. The hyaluronic acid present in the final composition may have a molecular weight ranging from 200 to 750 KD [[~~KDs~~]], preferably from 500 to 700 KD [[~~KDs~~]], and may be present at a percentage varying between 0.1 and 40%, preferably between 5 and 10%.

Please amend the paragraph at page 14, lines 1-5, as follows.

- ~~Hyaff~~ HYAFF® 11 with a percentage of esterification of between 55 and 100%;
- fibrin glue,
- photocross-linkable polymers (international patent application No. WO 03/076475),
- collagen and derivatives.

Please amend the paragraph at page 14, lines 17-18, as follows.

Lastly, the structures can also be sewn with suture thread based on ~~Hyaff~~ HYAFF® or another biocompatible and bioabsorbable polymer.

Please amend the paragraphs at page 15, lines 6-28, as follows.

Example 1

Preparation of the compact films constituted by ~~Hyaff~~ HYAFF® 11 as the outer layer/s of the new multilayer, composite structures

One litre of a solution of ~~Hyaff~~ HYAFF® 11 in DMSO (European patent No. 0216453 B1) is prepared at a concentration of 150 mg/ml.

Using a geared metering pump, the solution is passed through an extruder with a slit 20 cm long and

200 μm wide; the extruder is immersed in a coagulating bath constituted by 10 litres of ethanol-water at a ratio of 90:10.

The solid film that is formed is then passed into two subsequent baths filled with, respectively, ethanol-water at a ratio of 80:20 and ethanol alone.

Lastly, the film is dried and cut to size.

Example 2

Preparation of sponges of ~~Hyaff~~ HYAFF® 11 containing granules of hydroxyapatite and/or DM and/or other different biocompatible and biodegradabile ceramics

230 g. of sodium chloride crystals with a granule size of between 200 and 350 μm is mixed with 6.6 g. of citric acid with a granule size of less than 200 μm and with 8.5 g. of bicarbonate of soda with a granule size of between 140 and 400 μm.

The mixture is then supplemented with 20 g. of resorbable hydroxyapatite in granules sized 200-250 μm (or more), and/or DM and/or tribasic calcium phosphate and/or calcium sulphate.

Said mixture of salts is then further supplemented with 60 ml of a solution of ~~Hyaff~~ HYAFF® 11 in DMSO at a concentration of 180 mg/ml, and the components are mixed for at least 1 hour.

Please amend the paragraph at page 16, lines 8-16, as follows.

Example 3

Preparation of sponges of ~~Hyaff~~ HYAFF® 11 containing granules of hydroxyapatite subsequently coated/incorporated by ~~Hyaff~~ HYAFF® 11

Once the sponges have been prepared as described Example 2, and before they are freeze-dried, the product is immersed in 1 litre of solution constituted by ~~Hyaff~~ HYAFF® 11 esterified to a degree of 50% (~~Hyaff~~ HYAFF® 11p50) in water at a concentration of 9 g./l. Subsequently, said solution is de-

pressurised with a vacuum pump set at a pressure of less than 800 mbar for at least 0.5 minutes then returned to ambient pressure.

Please amend the paragraph at page 16, lines 19-23, as follows.

Example 4

Preparation of composite matrices of hydroxyapatite and/or of bone structures, containing/incorporating cross-linked hyaluronic acid (ACP®)

1.9-2 g. of hyaluronic acid salified with phenyl trimethyl-ammonium is solubilised in 27-30 ml of water.

Please amend the paragraph at page 17, lines 10-14, as follows.

It is heated to 62 °C for 12 hours, to obtain a product constituted by pieces of hydroxyapatite incorporated into/ or coated by a sponge of cross-linked hyaluronic acid (ACP®) which must immediately be washed in 3% ammonium acetate, ethanol, in 3% sodium chloride, and lastly in ethanol/water again to eliminate all traces of the sodium chloride.

Please amend the paragraph at page 17, lines 27-28, as follows.

The spongy structure thus obtained is placed between two layers of non-woven fabric constituted by ~~Hyaff~~ HYAFF®11p80.

Please amend the paragraphs at page 17, line 32 through page 18, line 31, as follows.

Example 6

Preparation of multilayer, composite structures in the final stage of assembly and fixing of the

inner matrix with the external layer.

Having prepared the matrix as described in examples 2, 3 and 4, it is wetted with ethanol and a thin layer of ~~Hyaff~~ HYAFF® 11 in DMSO at a concentration of 50 mg/ml is spread over the surfaces.

The surfaces thus prepared are then coated with the material of choice (non-woven fabric, or tissue or film, preferably of ~~Hyaff~~ HYAFF® 11), exerting slight pressure on it.

The product is then immersed in a bath of ethanol-water 80:20 for 1 hour and then washed repeatedly with pure ethanol.

The final composite product is washed in water and freeze-dried.

Example 7

Preparation of multilayer, composite "sandwich" structures, whose inner matrix contains ~~Hyaff~~ HYAFF®, hyaluronic acid and DM

3.6 g. of ~~Hyaff~~ HYAFF® 11p75 fibre is mixed for at least 10 minutes with 84 cc of a solution constituted by hyaluronic acid in an aqueous solution with a concentration of 18-19 mg/ml.

Said mixture is supplemented with 20 g. of granules of DM and kneaded for at least 15 minutes.

The paste thus obtained is subsequently spread into squares measuring, for example, 10x10 cm with a thickness of 2-3 mm.

The inner matrix thus formed is placed between 2 layers of ~~Hyaff~~ HYAFF® 11, made into a non-woven or woven fabric, having equal dimensions ~~aventi uguali dimensioni~~ and the composite multi-layer product obtained is calendered and finally freeze-dried.

The freeze-dried pieces can be cut to size.

At this point, the pieces can be treated by one or other of the following procedures:

1) both of them can be immersed in a solution of ~~Hyaff~~ HYAFF® 11p75 in DMSO with a concentration of 20-25 mg/ml for several minutes.

2) The edges of each piece can be wetted with a solution of ~~Hyaff~~ HYAFF® 11 in DMSO (with a concentration of 30-40 mg/ml) and subsequently immersed in an ethanol bath for at least 10 minutes.

Please amend the paragraphs on page 19, lines 5-16, as follows.

Example 8

Preparation of multilayer, composite "bag-shaped" structures

3.6 g. of ~~Hyaff~~ HYAFF®11p75 fibres are mixed for at least 10 minutes with 84 cc of a solution constituted by hyaluronic acid in an aqueous solution with a concentration of 18-19 mg/ml.

Said mixture is supplemented with 20 g. of granules of DM and kneaded for at least 15 minutes.

The paste thus obtained is inserted in a woven, tubular structure, preferably made of ~~Hyaff~~ HYAFF® 11, and freeze-dried.

The edges are then wetted with a solution of ~~Hyaff~~ HYAFF®11 in DMSO with a concentration equal to 35 mg/ml, and then immersed in an ethanol bath for at least 10 minutes.